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TITLE: Nebraska Prostate Cancer Research Program

PRINCIPAL INVESTIGATOR: Ming-Fong Lin

CONTRACTING ORGANIZATION: University of Nebraska
Omaha, NE 66196

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PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

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14. ABSTRACT

Prostate cancer (PCa) remains as one of the major cancers threatening US males' life. Better understanding the basic mechanism of this cancer is needed for developing more effective treatments, which would depend on the training of PCa researchers. This proposal is thus to train HBCU undergraduate science majors in PCa research, a joint effort between the University of Nebraska Medical Center (UNMC) and Clark Atlanta University (CAU). Drs. Ming-Fong Lin of UNMC and Dr. Shafiq Khan of CAU have ongoing research collaborations. They will identify interested undergraduates at CAU and institute a summer research program at UNMC where the students will do basic science or translational research in a laboratory. Students will spend the majority of their time working at the bench on a research project. They will also participate in a seminar series that will introduce them to different areas of scientific investigation and advanced technological tools used in scientific discovery. After the summer, students will continue their scientific development at CAU, preparing for a graduate career in biomedical sciences or for medical school.

15. SUBJECT TERMS

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Annual Summary

INTRODUCTION:

The subject of this training grant is to train potential prostate cancer (PCa) researchers via a collaborative effort between University of Nebraska Medical Center (UNMC) at Omaha, NE, and Clark Atlanta University (CAU) at Atlanta, GA. The conception of this Program is based on interactions and collaborations between Dr. Ming-Fong Lin, the PI and a faculty mentor at UNMC, and Dr. Shafiq Khan, a faculty mentor at CAU, since March 2004. The purpose of this proposal is to train undergraduate HBCU students to gain hand-on experience in performing PCa research in a research-intensive environment at UNMC. The scope of training grant is to train CAU undergraduate students to gain hand-on experience in PCa research at UNMC Nebraska Prostate Cancer Research Program (NPCRP). These students will receive training not only in the lab but also in the class room in the format of seminars and visiting biotechnology companies. The goal is to encourage and to prepare those HBCU students for academic career, i.e., they will either enter graduate school or medical school with training in, and understand of, prostate cancer research or enter medical school. This will increase the number of PCa researcher at both the basic science and the clinical science levels.

BODY:

During the past one year (4/2010 – 4/2011) with the funding support from CDMRP, we have trained 4 CAU undergraduate students, and these students have gained hand-on experience in PCa research and made significant accomplishments. There were no technical or unexpected difficulties encountered and/or any deviations from the original Statement of Work. Per Instruction, our training and research accomplishments following each task outlined in the approved Statement of Work are listed as follows:

Task 1: Announcement of the Year 1 Research Program (months 1-3)

Done. Per approved SOW, upon receiving the award notice, Drs. Khan and Odero-Marah at CAU announced the opportunity of conducting PCa research at UNMC, including verbal announcements in their classes during his lectures and also campus-wide posters by Dr. Khan's office. Ms. Priscilla Bakari, the Office Manager, helped prepared all the necessary documents and answered to all questions related to this opportunity. The announcements included the criteria of eligibility, the requirement of documents, and the due date of application.

Task 2: Selection of Trainees (month 4-6)

Done. Drs. Khan and Odero-Marah and Ms. Bakari at CAU went through all application files to ensure all application documents are complete and in place. Due to a short time period between the awarding letter and the student recruitment process, many communications were made possible through phone calls and e-mails. Subsequently, Drs. Lin and Chaney visited CAU, met with Drs. Khan and Odero-Marah, discussed application files and interviewed some eligible student candidates on March 17, 2010. The successful applicants were notified by e-mails and posted the list on board in CAU Prostate Cancer Research Center. The students were given a due date for replying of their acceptance, and all students accepted the offer by April 13, 2010.

In lab assignments, to avoid any potential of conflict of interest, upon request by Dr. Lin, Dr. Chaney coordinated with Dr. Odero-Marah considering students' interests with their priorities in lab selection and made the final matches as follows: Ms. Kiedra Bryant – Dr. MacDonald, Ms. NeChelle Jack – Dr. Lin, Ms. Lynnette Leffall – Dr. Mehta and Ms. Brittany

Jones – Dr. Batra. In the mean time, Dr. Chaney also worked out the Housing for students and coordinated with Ms. Jennifer Pace, the BMB Office Personnel, preparing all necessary documents for students.

Task 3: Summer Research (month 7-9)

Done. All students arrived on May 31, 2010, and Dr. Chaney picked them up at airport, went grocery shopping and settled down in the dorm. Drs. Chaney and Lin had dinner together with all students and provided them with the up-dated information and guidelines for the Program. Dr. Chaney attended students' Monday seminars, which were in conjunction with INBRE program, and both Drs. Chaney and Lin met with students weekly.

Upon arrival, the students were encouraged to set up a web for the Program. With the support of Jennifer and the UNMC Public Affair Office, the web for NPCRP was finalized and posted in BMB Department web by the end of June 2010. The link is as follows: (http://www.unmc.edu/biochemistry/index.cfm?L1_ID=48&CONREF=84). (**Appendix #1**).

Dr. Odero-Marah was invited to visit UNMC on July 6. She gave a scientific presentation on her research project entitled "Snail Transcription Factor Contributes to Prostate Cancer Tumor Progression via Reactive Oxygen Species", which was excellent and well received by audience. She then met with CAU students and had a lunch together to learn their progresses and to discuss any potential problem during their stays. Subsequently, Dr. Odero-Marah met with Drs. Lin and Chaney for an executive meeting discussing students' issues. While there was one suggestion regarding the payment method for housing; overall, all four students were very happy, enjoyed their stays and had obtained the hand-on experience in their research projects.

The efforts of NPCRP received attention. Dr. Chaney coordinated the efforts and the UNMC Public Affair Office interviewed all four CAU students and reported our Program with Ms. Lynnette Leffall in Dr. Mehta's lab as an example for the story (**Appendix #2**). All students prepared their posters and gave presentations in the UNMC Summer Undergraduate Research Program (SURP) poster section on Thursday of Aug. 5, 2010. The abstracts of posters are attached (**Appendix #3**).

Task 4: Evaluation of the Program (month 10-12)

Done. Prior to their departure, all four students met with Drs. Chaney and Lin and other faculty mentors, including Drs. Batra, MacDonald and Mehta, for a final lunch-meeting on Friday of August 6, 2010. We discussed any problem that occurred during their stays and any suggestions that may improve the training by the Program. In the meeting, all students received a certificate for their hard working with the completion of training, cosigned by Drs. Chaney and Lin. The anonymous evaluations that were made by students one week ahead are attached (**Appendix #4**).

Drs. Khan and Odero-Marah and Ms. Bakari met with students at CAU on September 2, 2010, the beginning of Fall semester. The students are very excited by the opportunity of training at UNMC. A Minute taken by Ms. Bakari is attached (**Appendix #5**).

Dr. Chaney met with Dr. Jim Turpen, a member of Executive Committee for NPCRP and the PI of the INBRE program, regarding the results of NPCRP training program during their INBRE Retreat. With Dr. Turpen's approval, the support from the INBRE program to NPCRP is highly appreciated. We expect continued interactions for the up-coming years.

Drs. Chaney and Lin met and discussed the questions raised by the students and the potential improvement for new students in the summer of 2011.

Task 5: Announcement of the Year 2 Research Program (months 13-15)

Done. Per approved SOW, Drs. Khan and Odero-Marah at CAU announced the opportunity of conducting PCa research at UNMC, including verbal announcements in their classes and also campus-wide posters by Dr. Khan's office in Feb 2011. Ms. Bakari, the office manager, prepared all the necessary paper works and answered to all questions related to this opportunity. The announcements included the criteria of eligibility, the requirement of documents, and the due date of application. For this cycle, the final due date was set as by March 31, 2011.

Task 6: Selection of Trainees (month 16-18)

Drs. Chaney visited CAU on March 29, 2011. He went alone, met with several student candidates and discussed with Dr. Odero-Marah and Ms. Bakari for student recruitment processes. Drs. Odero-Marah sent all information by March 31, 2011, the due date of application to Dr. Chaney. This year, we had 8 students completed their applications. Drs. Odero-Marah and Chaney discussed all the applicants' qualification and made offers to 4 students. All four students accepted the offer. Drs. Odero-Marah and Chaney have worked together and matched these students with mentors in NPCRP at UNMC. Dr. Chaney has also coordinated the Housing issue, and Ms. Pace had mailed the first batch of documents including Housing to students for their attention.

With the support of Dr. Turpen, the NPCRP will again interact with the INBRE program for student training in seminars and site visiting to various research facilities and biotech companies. Currently, we are waiting for the arrival of the new students.

Task 7: Summer Research (month 19-21) - Task 12: Evaluation of the Program (month 34-36)

To be accomplished in the up-coming summer.

KEY RESEARCH ACCOMPLISHMENTS:

- We successfully recruited 4 excellent HBCU undergraduate students from CAU in the first year of award.
- Based on their research interests, these four students were assigned to different labs with matched expertise in prostate cancer research for their respective prostate cancer research training.
- All four students attended the Monday seminar jointly with the INBRE program through the entire period.
- The students also visited different research institutions and BioPharm companies locally to expand their knowledge and scopes in future career developments.
- These CAU students also attended the seminars set by the UNMC SURP every Tuesday at noon through the entire training period.
- By attending the INBRE and the UNMC SURP activities, the students expand their view and social activities to different student communities.

- Dr. Lin attended the Undergraduate Student Luncheon and Networking Session in the IMPaCT meeting on March 11, 2011, interacting with other program leaders and students to learn more about the potential significance of this training program.

REPORTABLE OUTCOMES:

- The students actively worked together with BMB Personnel and with the support of UNMC Public Affair Office, a web for our NPCRP training program was prepared and posted on the BMB at UNMC web. The link is as follows: (http://www.unmc.edu/biochemistry/index.cfm?L1_ID=48&CONREF=84).
- UNMC Public Affairs reported the NPCRP program with one student as the story.
- As a part of training and requirement, all four students prepared their results and gave poster presentations jointly in the UNMC SURP poster section, the last Thursday of their training.
- All four students submitted their abstracts to the DOD PCa IMPaCT meeting at Orlando, FL, March 9-12, 2011.

CONCLUSION:

The purpose of this award is to train HBCU undergraduate students from CAU to gain hand-on experience in performing PCa research in a research-intensive focus group, the UNMC Nebraska Prostate Cancer Research Program (NPCRP). We are very pleased with the outcomes for the success of the first year training at UNMC. These students have received training not only in the lab but also in the class room in the format of seminars and visiting biotechnology companies. Our goal of training is to encourage and to prepare HBCU undergraduate students for academic career in graduate school or medical school with training in, and understand of, prostate cancer research. We propose that by this way, we can increase the number of PCa researcher from the minority group at both the basic science and the clinical science levels. With the first year of award support from the DOD PCa Research Program, as evidenced by the scientific outcomes of student posters and student comments, we are very excited by the success of our training program. We are expecting that more exciting results will be done in the up-coming years of the support.

REFERENCES:

1. Brittany T. Jones, Poomy Pandey, Srustidhar Das and Surinder K. Batra. (2010) Therapeutic Potential of Curcumin: Inhibition of MIC-1/GDF-15 Expression in Prostate Cancer Cells Exposed to Heavy Metal Carcinogen.
2. Keidra A. Bryant, Joseph R. Wheeler, Michelle A. Montgomery, Richard G. MacDonald. (2010) Effect of Metal Ion Chelators on Mannose 6-Phosphate/Insulin-like Growth Factor II Receptor in DU145 Prostate Cancer Cells.
3. Lynnette Leffall, Kristen E. Johnson, Parul Katoch, Linda Kelsey, and Parmender Mehta. (2010). Aspects of Gap Junction Assembly and Disassembly in Prostate Cancer Progression.
4. NeChelle L. Jack, Yu Wei Chou, Laurenee London, Xiu R. Bu, Ming-Fong Lin. (2010). The Effect of 4'-Bis-Thiosemicarbazide, a New Ribonucleotide Reductase Inhibitor, on Prostate Cancer Cell Proliferation.

APPENDICES:

1. Appendix #1: The web information for NPCRP posted on the BMB at UNMC web is attached.
2. Appendix #2: UNMC Public Affairs reported NPCRP student.
3. Appendix #3: Four abstracts prepared by the four CAU students are attached.
4. Appendix #4: Evaluation by the students upon their completion of training at UNMC prior to their departure.
5. Appendix #5: A Minute taken by Ms. Bakari at CAU for students' evaluation and comments during the meeting after their return to CAU.

Appendix #1

http://www.unmc.edu/biochemistry/index.cfm?L1_ID=48&CONREF=84

Nebraska Prostate Cancer Research Program (NPCRP)

This program is supported by the Department of Defense Prostate Cancer Research Program - Grant PC094595

Overview of NPCRP

Nearly 200,000 men in the U.S. will be diagnosed with prostate cancer and over 30,000 will die of this disease annually. While surgery and chemotherapy can cure the disease, in many cases it will spread and kill the patient. Better basic scientific understanding of this disease is needed to enable the development of more effective preventive and therapeutic treatments toward this cancer.

The development of better prostate cancer treatments depends on the training of prostate cancer researchers. This program is designed to train undergraduate science majors in prostate cancer research. It is a collaborative effort between the University of Nebraska Medical Center (UNMC), Omaha, NE and Clark Atlanta University (CAU), Atlanta, GA. Dr. Ming-Fong Lin of UNMC and Dr. Shafiq Khan of CAU have ongoing research collaborations. They will identify interested undergraduates at CAU for summer research at UNMC where the students will do basic science or translational research in a laboratory. Students will spend the great majority of their time working at the bench on a research project. They will also participate in a seminar series that will introduce them to different areas of scientific investigation and advanced technological tools used in scientific discovery.

After the summer, the students will continue research in a prostate cancer lab at CAU. They will thus continue their scientific development throughout the academic year in preparation for a graduate career in the biomedical sciences or for medical school.

Mission Statement of NPCRP

This Program will train undergraduate students to perform prostate cancer research in a research-intensive environment. They will continue to perform research during their undergraduate academic career. After graduation, the student participants will be prepared to enter graduate school or medical school with training in, and understanding of, prostate cancer research. This will increase the number of prostate cancer researchers in both the basic and the clinical sciences.

Focus Areas of Research in NPCRP

Since our faculty members are engaged in a variety of research projects, students will have the opportunity to be trained in different areas of prostate cancer research. For example, the focus areas or research include Biomarkers, Therapy, Genetics, and Tumor Biology as outlined by the laboratory research descriptions in the table below.

NPCRP: Program Director, Staff Members and Mentors

Dr. Ming-Fong Lin, PD/PI of NPCRP, has served as the Coordinator/Leader of the UNMC Eppley Cancer Center Prostate Cancer Research Focus Group since 1997. Dr. Lin is a veteran in prostate cancer research for over twenty years. He was initially involved in the early investigation on the potential of prostate-specific antigen (PSA) as a surrogate marker for prostate cancer, comparing with the classical marker, circulating prostate acid phosphatase (PAcP). For investigating the molecular mechanism of hormone-refractory prostate cancer progression, Dr. Lin has established clinic-relevant, U.S. patent-awarded prostate cancer cell lines, which are well accepted by scientists in the field. Dr. Lin has also made the seminal discovery on the novel role of cellar PAcP in prostate cancer progression, corroborating clinic phenomena. Since 1995, he has served in various study sections for National Institutes of Health, Department of Defense Congressionally Directed Prostate Cancer Research Program, American Cancer Society and others.

The concept of training of undergraduate HBCU students from CAU is based on long-term interactions between Dr. Lin and Dr. Shafiq Khan, the faculty mentor at CAU. Dr. Lin has been a member of the Executive Advisory Committee for the NIH Research Center in Minority Institute (RCMI) at CAU and Dr. Khan is the Director of the Center since March 2004. Recently, Dr. Khan's Center, with Dr. Lin's inputs, was awarded a grant from NIH National Center on Minority Health and Health Disparities (NCMHD) for establishing a Center of Excellence for Prostate Cancer Research, Education and Services at CAU. To strengthen the research efforts in prostate cancer at CAU, Dr. Lin has provided necessary expertise and reagents to Dr. Khan and his faculty members. Dr. Lin and Dr. Khan have research collaborations as well; Dr. Lin is a consultant in Dr. Khan's DOD PCa Idea Award which has resulted in a co-authored publication in 2008 and additional collaborative articles are under construction or pending reviewing.

Dr. William Chaney serves as the Program Coordinator organizing orientation sessions and a summer seminar series for the students. He has over fifteen years of experience with undergraduate summer programs, having organized the first one provided by the College of Medicine at UNMC. He currently is the Program Coordinator of the NIH-supported Nebraska Center for Functional Genomics INBRE grant (The P.I. of the grant is Dr. James Turpen of UNMC). In this role, he organizes summer orientation and seminar presentations for undergraduate students. The concept is supported by Dr. Turpen, and the CAU students will also attend the INBRE activity during their summer research at UNMC. Thus, Dr. Chaney brings a tremendous amount of experience and activities to the CAU students in the NPCRP.

In NPCRP, fourteen faculty members from Creighton University (CU) in Omaha; University of Nebraska – Lincoln (UNL) and University of Nebraska Medical Center (UNMC) have agreed to serve as potential research mentors for this proposal. Their research areas cover a wide range of expertise and interest in cancer research including prostate cancer (the detail of research activity is described in the table below). Thus, a student entering this program can find a research mentor who is working in an area of interest to that student.

Faculty Advisors at CAU

Dr. Shafiq Khan, Professor of Biological Sciences at CAU, will serve as the faculty advisor for the undergraduate students participating in this program. He currently coordinates undergraduate research efforts at CAU and is extensively involved in their research experiences. Dr. Khan is the Director of Research Center in Minority Institute (RCMI) program and also is the PI of the Prostate Cancer Research Center at CAU supported by NCMHD, NIH. Dr. Khan has an active research lab and is funded externally including the DOD Prostate Cancer Research Program Idea award. To strengthen the effort of this training program, upon discussion with Dr. Lin, Dr. Khan recruited Dr. Valerie Odero-Marah, Assistant Professor of Biology at CAU, who is also funded by the DOD Prostate Cancer Research Program to serve as the Program Coordinator supporting Dr. Khan in student recruitment and mentoring at CAU.

Research Mentors and Projects

Investigator	**Institution**	**Project**
S. Batra	UNMC	Genetic Alterations in Prostate Cancer Progression
J. Christman	UNMC	Regulation of DNA Methylation in Prostate Cancer
W. Chaney	UNMC	Glycobiology in Prostate Cancer
P. Cheng	UNMC	Glycomics in Prostate Cancer Metastasis and Gene Therapy
J. Davis	UNMC	Hormone Regulation of Tumor Cell Development
R. Lewis	UNMC	IGF Receptors in Prostate Cancer
M.-F. Lin	UNMC	Androgen Regulation of Prostate Cancer Growth and Development
R. MacDonald	UNMC	IGF Axis in Prostate Cancer Growth
P. Mehta	UNMC	Gap Junction Proteins in Prostate Cancer Metastasis
E. Rogan	UNMC	Metabolism of Dietary and Environmental Chemicals to Mutagenic and Genotoxic Species
M. Simpson	UNL	The Role of Hylauronate in Prostate Cancer Development

R. Singh	UNMC	Prostate Cancer Metastasis and Immunology
Y. Tu	CU	Regulation of G-Protein-Coupled Receptors in Prostate Cancer
D. Wang	UNMC	Targeted Therapies for Prostate Cancer Bone Metastasis

2010 INBRE-BRIN Scholars First Week Schedule

Michael Sorrell Center Room 2010
UNMC

Tuesday-June 1

8:00	Welcome and Introductions	J. Turpen P. Davis
9:00	Use of Animals in Research	J. Turpen
9:45	Laboratory Safety	W. Chaney
10:45	Introduction to Bioinformatics	H. Ali
12:00	Lunch	
1:00	Library Access	M. Helms
1:45	Responsible Conduct in Research	D. Crouse
2:30	Sequence Analysis Tools	D. Bastola
3:45	Radiation Safety Usage and Video	W. Chaney
4:45	Wrap-up and Questions	
5:30	Barbeque Welcome Banquet	J. Turpen

Wednesday-June 2

9:00	Science as a Career	D. Crouse
9:50	Graduate Studies at UNMC	A. Schlueter
10:30	MD/PhD Program at UNMC	S. Smith
10:50	Graduate Studies at Creighton	R. Murphy
11:20	Graduate Studies at UNL	J. Morris
12:00	Lunch	
	Go meet mentors and labs.	

2010 INBRE Weekly Seminar Schedule
(all on Mondays)

June	7	UNL	9:00	J. Morris	Beadle Center
June	14	UNMC	9:00	P. Ciborowski	UNMC Proteomics Core
			10:30	K. Bayles	Control of Clinically Important *Staphylococcus* Infections
June	21	CU	9:00	S. Lovas	Structural Proteomics and Bioinformatics Research
			10:15		Lab Tours
			11:00	L. Bruce	Evolution of Brain Development
June	28	Lincoln Biotech	9:00	Ian Davis	Drug Development/Analysis at Celerion Corp. (MDS-Pharma)
July	5	No Seminar			
July	12	Omaha Biotech	9:00	M. Dixon	Patent Development at UNEMED
			10:30	T. Wasmoen	Vaccine Research/Development at Intervet/Schering-Plough
July	19	UNMC	9:00	J. Eudy	UNMC DNA Analysis Core
			10:30	D. Romberger	Pulmonary Disease and Research
July	26	UNL	9:00	J. Morris	Morrison Center
Aug	2	CU	9:00	G. Soukup	MicroRNA Function in Neurosensory Development
			10:15		Lab Tours
			11:00	R. Hallworth	The Life and Death of Hair Cells

2010 Summer Undergraduate Research Program

Date	Title and Speaker	Location	Time
Wednesday, June 2nd	**Welcome Reception** Speaker: Dr. Rubens Pamies	DRC I 1002 Auditorium	11:00 am
Wednesday, June 2nd	**Compliance Training** Registration begins at 12:30 pm	DRC I 1002 Auditorium	1:00 pm
Tuesday, June 8th	**Luncheon Seminar** Speaker: Dr. Paul Dunman	ESH 3010 Auditorium	12:00 pm
Tuesday, June 15th	**Luncheon Seminar** Speaker: Dr. Steven Caplan	ESH 3010 Auditorium	12:00 pm
Tuesday, June 22nd	**Luncheon Seminar** Speaker: Dr. James Haorah	ESH 3010 Auditorium	12:00 pm
Tuesday, June 29th	**Luncheon Seminar** Speaker: Dr. Jenny Wang	ESH 3010 Auditorium	12:00 pm
Tuesday, July 6th	**Luncheon Seminar** Speaker: Dr. Jennifer Larsen	ESH 3010 Auditorium	12:00 pm
Tuesday, July 13th	**Luncheon Seminar** Speaker: Dr. Tammy Kielian	ESH 3010 Auditorium	12:00 pm
Tuesday, July 20th	**Luncheon Seminar** Speaker: Dr. Howard Fox	ESH 3010 Auditorium	12:00 pm
Tuesday, July 27th	**Luncheon Seminar** Speaker: Dr. Joseph Vetro	ESH 3010 Auditorium	12:00 pm
Thursday, August 5th	**SURP Poster Presentation**	DRC I Atrium	10:00 am
	SURP Reception & Certificate Presentation	DRC II Commons Area	12:30 pm

UNIVERSITY OF Nebraska Medical Center

Clark Atlanta University Students

**We would like to acknowledge Lisa Spellman and the Public Relations Office for taking the photos below of the Clark Atlanta University Students (group photo and four head shots). We appreciate their support.

Lynnette, Leffall, Brittany Jones, Nechelle Jack, Keidra Bryant

Keidra Bryant

Senior Undergraduate Student majoring in Biology

After receiving her B.S. degree, she plans on obtaining an MD/PhD degree. She has a strong passion for research on prostate cancer and plans to continue her journey working with it. She is currently working in Dr. Richard MacDonald's lab, where her main focus is on DU145 cells and trying to see if IGFII is important in prostate cancer and if it will maintain cell growth. She plans on continuing her work on prostate cancer while at Clark Atlanta University.

Nechelle Jack

Senior Undergraduate Student majoring in Biology
She is interested in prostate cancer research.
After receiving her B.S., she plans on obtaining a MD/PhD degree or becoming a Physician's Assistant. She is currently working in Dr. Ming-Fong Lin's lab and the basis of her project is to observe "the effect of anti-cancer compounds in prostate cancer cells." She is excited to see the results of this project and feels very blessed and honored to be given such an amazing opportunity. She would like to thank Dr. Lin of UNMC and Dr. Khan of CAU - she would not be here without them!

Brittany Jones

Senior Undergraduate Honors Student majoring in Biology
After receiving her B.S., she plans on matriculating into a MD/PhD program. She has a strong passion for finding a cure for cancer. She enjoys doing research because research is to see what everybody else has seen and to think what nobody else has every thought. She's currently working in Dr. Surinder K. Batra's lab, where her research project is to monitor "What effect do Curcumin, $NiCl_2$, and $CoCl_2$ has on PC3M, LnCap, RWPE1, and PC3 cell lines." She plans on using the knowledge gained during this program and apply it when she returns to Clark Atlanta University.

Lynnette Leffall

Senior Undergraduate Student majoring in Biology
After receiving her B.S., she plans on obtaining an MD/PhD degree and concentrating on clinical research dealing with different forms of cancers as well as practicing medicine. She is currently working in Dr. Parmender Mehta's lab looking at the trafficking of Cx26 in BxLx26 Z-3 pancreatic cancer cell lines comparative to LNCaP26 prostate cancer cell lines. At the end of this summer, she hopes to understand the importance that Cx26 plays in both cancer cells.

Kristen Johnson and Lynnette Leffall, Mehta Lab

Poomy Pandey and Brittany Jones, Batra Lab

Keidra Bryant and Joe Miller, MacDonald Lab

Nechelle Jack and Yu-Wei Chou, Lin Lab

Nebraska Prostate Cancer Research Program (NPCRP)

http://www.unmc.edu/biochemistry/index.cfm?L1_ID=48&CONREF=84

Funding:
Department of Defense
Prostate Cancer Research Program,
the Office of the Congressionally Directed Medical Research Programs (CDMRP)
(***Grant #: PC094594***)

Collaborations:
Dr. Ming-Fong Lin and Dr. William Chaney,
University of Nebraska Medical Center (UNMC),
and
Dr. Shafiq Khan and Dr. Valerie Odero-Marah,
Clark Atlanta University (CAU)

Supported by
Department of Biochemistry & Molecular Biology, UNMC
Nebraska Center for Functional Genomics
NIH INBRE Program
Drs. Batra, Cowan, Pamies, and Turpen

Faculty members:
Creighton University (CU) at Omaha;
University of Nebraska – Lincoln (UNL) and
University of Nebraska Medical Center (UNMC)

University of Nebraska Medical Center

Department of Biochemistry &
Molecular Biology

Seminar Series

"Snail Transcription Factor Contributes to Prostate Cancer Tumor Progression via Reactive Oxygen Species"

Presented by

Valerie Odero-Marah, PhD
Assistant Professor
Department of Biology
Clark Atlanta University

****Supported by the Department of Biochemistry & Molecular Biology and the Nebraska Prostate Cancer Research Program****

Tuesday, July 6, 2010

3:00 p.m.

DRC1 Room1004

Acknowledgements:

CAU students:
Keidra Bryant:
Joe Miller in Dr. MacDonald's Lab

Nechelle Jack:
Dr. Yu-Wei Chou in Dr. Lin's Lab

Brittany Jones:
Poomy Pandey and Srustidhar Das in
Dr. Batra's Lab

Lynnette Leffall:
Kristen Johnson in Dr. Mehta's Lab

Supports:
BMB, UNMC
Ms. Amy Dodson, MBA
Ms. Jennifer Pace

CCRTD/RCMI Program, CAU
Ms. Priscilla Bakari, MA

DOD CDMRP PCa Program
Grant #: PC094594

Only@UNMC with Lynnette Lefall

You know them when you have them.

Maybe you're busy with a patient, working with a student or learning from a professor.

Immersed completely in the moment, it hits you, "This is where I'm supposed to be and this is what I'm supposed to be doing."

Lynnette Lefall

They are "Only@UNMC" moments -- born from the combination of people, place and purpose that exists only at UNMC.

Lynnette Leffall, a biology major from Clark Atlanta University who was one of four students to spend eight weeks at UNMC this summer working with investigators in the Nebraska Prostate Cancer Training Program, describes an Only@UNMC moment.

"This is my first year doing research, so when I came to UNMC I was a little intimidated. At Clark, I study biology but have never worked in a lab before. The other girls I came here with have all been in a lab. I felt like I had to step up my game just to keep up with them.

"All of that changed the day I learned how to split a cell line. I was so excited. Just seeing the cells come off the plate, seeing them grow and knowing I could take living cells and keep them alive. That was cool. I felt empowered, like I could do anything."

Share your "Only@UNMC" moments.

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Keidra Bryant – Abstract

Effect of Metal Ion Chelators on Mannose 6-Phosphate/Insulin-like Growth Factor II Receptor in DU145 Prostate Cancer Cells

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Joseph R. Wheeler, Michelle A. Montgomery, Richard G. MacDonald

The M6P/IGF2R is a multifunctional transmembrane receptor. The major function is to transport lysosome enzymes from where they are processed in the Golgi apparatus to the lysosomes.It is important for cells to maintain receptor expression on the cell surface for proper growth control and to prevent cancer. This includes prostate cancer. Prior work in the MacDonald laboratory showed that the receptor's ectodomain is cleaved at the cell surface by a protease that is inhibited by metal ion chelators. This work was done in a human embryonic kidney cell line. The goal of my project was to determine if this process also occurs in prostate cancer cells.
To address this question, we investigated whether metal ion chelators would inhibit this process in the insulin-like growth factor-responsive human prostate cancer cell line DU145. Cells were grown to 70-80% confluences and switched to serum-free medium for one day. Then, the cells were exposed to different concentrations of the chelators for 18-24 hours, scraped and processed for preparation of cell lysates and conditioned medium, which were analyzed for receptor amount by immunoblotting.
Immunoblot analysis indicated a concentration-dependent effect of the chelators 1,10-ortho-phenanthroline (OPA), Ethylenediaminetetraacetic acid (EDTA), Ethylene glycol tetraacetic acid (EGTA) to increase recovery of M6P/IGF2R in cell lysates. Of these reagents, OPA seemed to be the most effective, consistent with the hypothesis that metalloprotease responsible for cleaving the M6P/IGF2R ecodomain is Zn^{2+} -dependent.

NeChelle Jack - Abstract

The Effect of 4'-Bis-Thiosemicarbazide, a New Ribonucleotide Reductase Inhibitor, on Prostate Cancer Cell Proliferation

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Background: Although several approaches, including surgery and radiation therapy, provide physicians with options for treating patients with early stages of prostate cancer, no effective therapeutic treatment option for the advanced castration-resistant cancer is currently available. The development of new highly potent with low toxic chemotherapeutic agents as an effective treatment for prostate cancer with the castration-resistant phenotype is immediately needed. In this project, a new ribonucleotide reductase (RR) inhibitor, 4'-Bis-Thiosemicarbazide, was synthesized and tested to examine its effect on prostate cancer cell proliferation using the US Patent-awarded LNCaP cell model system.
Methods: The effect of 4'-Bis-Thiosemicarbazide on the proliferation of androgen-sensitive LNCaP C-33 and androgen-independent LNCaP C-81 prostate cancer cells was examined. C-81 cells exhibit many biochemical properties of prostate cancer cells at the castration-resistant stage. Cells were cultured in regular medium and also steroid-reduced condition, mimicking androgen-ablation therapy in clinics. The effect of 4'-Bis-Thiosemicarbazide at 1 and 10 µM concentrations on cell growth was analyzed by cell number counting, and the solvent DMSO was used as a control. The expression of cell proliferation markers including cellular prostatic acid phosphatase (cPAcP), an authentic protein tyrosine phosphatase functioning as a negative growth regulator, was also analyzed by western blot analyses.
Results: Upon 4'-Bis-Thiosemicarbazide treatment, the growth of LNCaP C-81 cells significantly diminished, followed a dose-dependent phenomenon under both regular and steroid-reduced conditions. In 4'-Bis-Thiosemicarbazide-treated LNCaP C-81 cells, cPAcP protein levels were elevated, inversely correlating with growth suppression. Interestingly, 4'-Bis-Thiosemicarbazide also reduced LNCaP C-33 cell growth in regular medium, while the expression level of cPAcP protein was not significantly altered.
Conclusion: Our results clearly show that 4'-Bis-Thiosemicarbazide exhibits an inhibitory effect on the proliferation of LNCaP C-81 prostate cancer cells, following a dose-dependent fashion. In those treated C-81 cells, cPAcP expression level is up-regulated. Further studies shall be continued to clarify the molecular mechanism of growth suppression and the potential of 4'-Bis-Thiosemicarbazide as a therapeutic agent on advanced castration-resistant prostate cancer.
(This project is supported in part by DOD PC094594 and NCI CA88184.)

Brittany Jones – Abstract

Therapeutic Potential of Curcumin: Inhibition of MIC-1/GDF-15 Expression in Prostate Cancer Cells Exposed to Heavy Metal Carcinogen

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Prostate cancer is one of the major cancer related deaths among American men. There is emerging evidence that prostate inflammation is one of the major factors contributing to prostatic carcinogenesis. Various proinflammatory cytokines, chemokines and other immune molecules are observed near tumor microenvironment and help in tumor proliferation. Macrophage inhibitory cytokine 1 (MIC-1) is a member of Transforming Growth Factor-β (TGF-β) family of cytokines and has been shown to inhibit the secretion of TNF-α by activated macrophages and thereby reduce the tumor killing activity of macrophages. MIC-1 has been shown to be overexpressed in prostate cancer and has been proposed to be used a prognostic and diagnostic marker of prostate cancer along with PSA (Prostate Specific Antigen). It has also been shown that MIC-1 is upregulated in response to hypoxia and anoxia. Promoter analysis of MIC-1 indicated the presence of putative consensus sequences for transcription factor binding elements such as NFkB. The role of NFkB in hypoxic stress has been demonstrated. At the same time Curcumin has been shown to inhibit the NFkB pathway in various cancer models. Therefore, we hypothesized that Curcumin can be used as a potential therapeutic agent in prostate cancer where it can downregulate MIC-1 production. We looked at the MIC-1 mRNA expression in various prostate cancer cells (PC3, PC3M, LnCap35 and LnCap126) upon treatment with $NiCl_2$ and $CoCl_2$. RWPE1, a benign immortalized prostatic epithelial cells, was also used, but had least MIC-1 mRNA in comparison to the cancer cells. mRNA expression was verified by both RT-PCR as well as quantitative real-time PCR. Because MIC-1 is a secretory cytokine, culture supernatants were checked for the secretory MIC-1 in two cell models i.e. PC3M and LnCap126 cells, and a similar induction was observed upon treatment with $NiCl_2$ and $CoCl_2$. When cells were treated with Curcumin, we observed a decrease in the MIC-1 expression compared to controls as well as cells treated with heavy metals. In addition, $CoCl_2$-induced motility of PC3 cells was inhibited by Curcumin. $NiCl_2$ had no effect on motility of PC3 cells. Various sequential and combinatorial treatment of $NiCl_2$ and Curcumin demonstrates the potential of Curcumin as a therapeutic target to be used in prostate cancer. In conclusion, we demonstrate the potential of Curcumin in downregulating MIC-1 expression induced by hypoxic condition and thereby can be a potential agent for prostate cancer therapy.

Lynnette Leffall – Abstract

Aspects of Gap Junction Assembly and Disassembly in Prostate Cancer Progression

Lynnette Leffall, Kristen E. Johnson, Parul Katoch, Linda Kelsey, and Parmender Mehta
Department of Biochemistry and Molecular Biology, University of Nebraska Medical Center

The prostate is composed of epithelial cells, which line the ducts and acini, and the mesenchymal cells, which form the stroma. Androgen-regulated stromal-epithelial interactions govern the proliferation, differentiation and apoptotic death of normal and malignant prostate epithelial cells. Androgens either act directly on luminal cells and/or indirectly via stromal cells through the release of paracrine mediators, such as growth factors. The incidence of prostatic cancer increases with age and is characterized by progression from a slow-growing hormone (androgen)-sensitive state to a highly malignant, hormone-independent state. In the absence of androgens, luminal cells of normal prostate, and malignant cells of prostate tumors, die by apoptosis. Gap junctional cell-to-cell channels provides a direct intercellular communication pathway for the growth regulatory signaling molecules (˜ 1000 D) and hence may be important in regulating prostate morphogenesis and oncogenesis. The gap junctional channels are bicellular structures formed by the members of related proteins named connexin (Cx)s, which first assemble into connexons that align and join with connexons in adjacent cells to form channels. We previously showed that the normal luminal cells or prostate express Cx32 and Cx26 whereas basal cells express Cx43. We have also shown that the trafficking and assembly off Cxs is impaired during prostate cancer progression (Govindarajan et al. *J Biol Chem*, 2002). We have also shown that reintroduction of Cx32 and Cx43 into Cx-deficient, indolent PCA cell line, LNCaP, retards growth and induces differentiation, whereas re-introduction of the same Cxs into an invasive cell line, PC-3, results in intracellular accumulation due to impaired trafficking (Mehta et al. *Dev Genetics*, 1999; Govindarajan et al. *J Biol Chem*, 2002). Significantly, our recent studies document that androgens regulated the formation and degradation of gap junctions (Mitra et al. *Mol Biol Cell*, 2006). Hence, elucidation of the molecular mechanisms of how gap junctions form and degrade may open up a therapeutic window to modulate prostate cancer growth and progression.

Please fill out and return to Dr. Lin.

1. How satisfied are you with the Nebraska Prostate Cancer Research (NPCRP) Scholars program?

(Very satisfied) Satisfied Dissatisfied Very dissatisfied

2. How did you originally learn about the NPCRP Scholars program?

I originally ~~heard of this~~ learned about this opportunity from Dr. Odero-Marah in Genetics class.

3. Did you have a clear set of expectations of the NPCRP program when you first became a NPCRP Scholar?

Yes. I expected to learn more about Prostate cancer at the microscopic level as well as research experience.

4. Was the process matching you with your mentor/advisor a good one?

Yes!

5. **How would you rate your research experience as it relates to helping you make decisions related to your education and career plans?**

I would rate my research experience increasingly high as it relates to making decisions career wise. I would honestly consider research & Medicine as a career option. This summer has shown me the importance research experience has on the world.

6. **What do you consider to be the main benefit(s) of the NPCRP Scholars program?**

I consider research exposure as the main benefit of the NPCRP Scholars Progam, particularily Prostate Cancer research exposure.

7. **What suggestions would you give for the program for next summer?**

More seminars based on Prostate Cancer as well as an introductory seminar to Prostate Cancer.

Please fill out and return to Dr. Lin.

1. How satisfied are you with the Nebraska Prostate Cancer Research (NPCRP) Scholars program?

Very satisfied *Satisfied* *Dissatisfied* *Very dissatisfied*

2. How did you originally learn about the NPCRP Scholars program?

Dr. Khan from Chalk Alpha University

3. Did you have a clear set of expectations of the NPCRP program when you first became a NPCRP Scholar?

Yes

4. Was the process matching you with your mentor/advisor a good one?

Yes it was a good match for me

5. **How would you rate your research experience as it relates to helping you make decisions related to your education and career plans?**

I would rate it on a scale of 10 an 9. It was very helpful in the decision about my education.

6. **What do you consider to be the main benefit(s) of the NPCRP Scholars program?**

The learning benefits that they had to offer.

7. **What suggestions would you give for the program for next summer?**

To let the student visit the lab ~~before and to in~~ when arriving and to also have a seminar about prostate cancer

Please fill out and return to Dr. Lin.

1. How satisfied are you with the Nebraska Prostate Cancer Research (NPCRP) Scholars program?

   Very satisfied ***Satisfied*** ***Dissatisfied*** ***Very dissatisfied***

   Satisfied.

2. How did you originally learn about the NPCRP Scholars program?

   - I heard it from my institution at Clark Atlanta University.

3. Did you have a clear set of expectations of the NPCRP program when you first became a NPCRP Scholar?

   At first, it wasn't vivid about the program. After coming here I gained insight about the expectation of the NPCRP.

4. Was the process matching you with your mentor/advisor a good one?

   yes, I loved working with my mentor as well as my advisor.

5. **How would you rate your research experience as it relates to helping you make decisions related to your education and career plans?**

I would rate it a 9 out of 10.

6. **What do you consider to be the main benefit(s) of the NPCRP Scholars program?** The main benefit of this program is to gain insight more about research and have a more hands on experience.

7. **What suggestions would you give for the program for next summer?**

My suggestion for the program is maybe have more activities throughout the week.

Please fill out and return to Dr. Lin.

1. How satisfied are you with the Nebraska Prostate Cancer Research (NPCRP) Scholars program?

Very satisfied (*Satisfied*) *Dissatisfied* *Very dissatisfied*

2. How did you originally learn about the NPCRP Scholars program?

At Clark Atlanta University. My advisor Dr. Bu informed me about the NPCRP Scholars Program along with Dr. Khan.

3. Did you have a clear set of expectations of the NPCRP program when you first became a NPCRP Scholar?

Yes and NO. I knew since the Program was new there would be some glitches that needed to be worked out. On the other hand, I had high expectations that the program would be a success, and that I would come out being a ~~better~~ scientist and scholar, then when I started.

4. Was the process matching you with your mentor/advisor a good one?

The ~~labs~~ participants should have been able to choose their labs once they get to UNMC.

5. **How would you rate your research experience as it relates to helping you make decisions related to your education and career plans?**

After being a participant in the NPCRP Program I believe my research experience is at a higher level, and I should not have any problems getting into graduate school.

6. **What do you consider to be the main benefit(s) of the NPCRP Scholars program?**

- Research Experience
- Attending Seminars
- Social Networking
- Working in a Professional environment
- Being Advised by award-winning, Intelligent mentors,

7. **What suggestions would you give for the program for next summer?**

- Allowing more students to be involved in NPCRP Program.
- Have NPCRP Stand alone as its own Program, not combining it with the INBRE Program
- Making sure students know exactly what they will be doing and making sure they have a strong understanding of what Prostate Cancer is.

Meeting with UNMC Summer Students
September 2, 2010

- Minutes taken by Ms. Priscilla Bakari

Present:
Dr. Shafiq A. Khan
Dr. Valerie Odero-Marah
Ms. Priscilla Bakari
Ms. Nechelle Jack
Ms. Brittany Jones
Ms. Keidra Bryant
Absent: Ms. Lynnette Leffall

Dr. Khan told students that this meeting was scheduled to gain feedback from them regarding their experience during the summer in Omaha. He asked each to delineate their thoughts on interactions with faculty and research staff in the perspective research laboratory and to give a summary of the highlights of their stay in Omaha. Below is a synopsis of their responses:

- All students said they had a great experience and would definitely recommend the program to other fellow students.
- All students said at first it was a difficult adjustment culturally, but everyone was very helpful and once they adjusted, they had a good time; they worked hard and learned a lot.
- All students said that they are able to continue their research from Omaha in the laboratories of CCRTD investigators at Clark Atlanta University.
- All students are applying to UNMC for the MD/PhD program.

Dr. Khan asked students to help recruit 4 new students for next summer and they agreed to help.

NOTE: Ms. Lynnette Leffall was not able to attend the initial meeting because of her class schedule however she met with Dr. Khan at a later time.